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5-20-97

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: New Chemical: Consideration of Conditional Registration for the New Chemical, Halofenozide, for Use on Turf grass (EPA File Symbol 69075-R, 69075-E,69075-G, and 69075-U.)

----------DECISION MEMORANDUM----------

FROM: James J. Jones, Acting Director
Registration Division

TO: Dan Barolo, Director
Office of Pesticide Programs

This memorandum recommends that you concur on the conditional registrations of **the manufacturing and end-use pesticide products which contain the new chemical, Halofenozide, Benzoic acid, 4-chloro-, 2-benzoyl-2-(1,1-dimethylethyl) hydrazide**, because these products meet the criteria for FIFRA Section 3(c)(7)(C) and are thus eligible for conditional registration. The applicable data requirements as put forth in 40 CFR Parts 150 to 189 have been adequately addressed for Section 3(c)(7)(C) registration under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for each of these products.

BACKGROUND

On June 26, 1995 RohMid, LLC. submitted applications for unconditional registration of a manufacturing use product (MUP) "Halofenozide Technical Insecticide" (EPA File Symbol 69075-R) and an end use product (EP) "Mach 2 Liquid Turf Insecticide" (EPA File Symbol 69075-E), respectively. A Federal Register Notice announcing receipt of these applications to register products containing a new active ingredient was published on February 14, 1996. No comments were received with respect to this notice. Subsequently, RohMid submitted two additional end use products (Mach 2 2.5% Granular Turf Insecticide and Mach 2 Granular Turf Insecticide).

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In their application for registration, RohMid LLC. requested that Halofenozide be considered as a Reduced-Risk pesticide. The Reduced-Risk Rationale submitted by RohMid LLC. was reviewed and accepted by the Agency. As a result, RD accelerated the review of this pesticide under the Voluntary Reduced-Risk Pesticide Initiative described in Pesticide Regulation Notice 93-9. However the reduced risk classification was withdrawn. This final determination was based on the rationale that Halofenozide was moderately to very persistent in soils and considerably mobile resulting in the potential for groundwater contamination.

PUBLIC INTEREST FINDING

A Public Interest Document was submitted by RohMid in support of Conditional Registration. This document was reviewed by the Biological and Economic Analysis Division. It was determined that it would be in the public interest to issue a Conditional Registration for the following reasons:

1. Halofenozide gives excellent control of turf grass insect pests.

2. Halofenozide exhibits a novel mode of action which does not disrupt beneficial insect populations.

3. Halofenozide can be used at lower rates than its alternatives for turf grass insect pests.

FORMULATION, USE PATTERN and PRODUCT LIMITATIONS

Halofenozide interferes with the action of the natural insect hormone,20-hydroxy ecdysone, the physiological inducer of the molting and metamorphosis process in insects. It primarily affects the larval stages of several orders of insects including many coleopterous and lepidopterous species and some homopterous and dipterous species. The end-use products consist of a soluble concentrate liquid product containing 22.3% by weight of the new chemical, halofenozide, a 2.5% granular product and a 1.5% granular product. The use pattern for these products is limited to turf grass.

SUMMARY and STATUS OF DATA REQUIREMENTS

Agency review of the product chemistry, toxicology, ecological effects, and environmental fate data have been completed and a summary assessment of these findings follows:

Scientific Findings

I. Product Chemistry

Product chemistry data: product identity/composition, analysis/composition, analysis/certification of ingredients and physical/chemical characteristics have been reviewed and are acceptable.

II. Toxicology

The Toxicology Branch has concluded that the data submitted are adequate for the registration of these products for turf grass use.

The following acute studies required for the proposed end-use product (Mach 2 Liquid Turf Insecticide) were reviewed and determined to be acceptable: acute oral toxicity (rat), acute dermal toxicity (rabbit), acute inhalation toxicity (rat), primary eye irritation (rabbit), primary dermal irritation (rabbit), and dermal sensitization (guinea pig). Based on these studies, the appropriate signal word is "CAUTION" (Toxicity Category III).

The following acute studies required for the proposed end-use products (Mach 2 2.5% Granular Turf Insecticide and Mach 2 Granular Turf Insecticide) were reviewed and determined to be acceptable: acute dermal toxicity (rabbit), primary eye irritation (rabbit), primary dermal irritation (rabbit) and dermal sensitization. The acute oral and inhalation studies were waived. Based on the reviewed studies, the appropriate signal word is "CAUTION" (Toxicity Category III).

The following acute studies required for the proposed Technical Halofenozide formulation were reviewed and determined to be adequate: acute oral toxicity (rat), acute dermal toxicity (rabbit), acute inhalation (rat), primary eye irritation (rabbit), primary dermal irritation (rabbit), and dermal sensitization (guinea pig). Based on these studies, the appropriate signal word is "CAUTION" (Toxicity Category III).

An acute oral neurotoxicity study in rats demonstrated a NOEL of 200 mg/kg. A LOEL of 400 mg/kg was determined based on increased mortality and clinical signs of toxicity (anogenital staining, red stained muzzle, scant feces and reaction to removal from cage).

In the feeding phase of a combined subchronic feeding/neurotoxicity study in rats, a tentative NOEL was determined to be 75 ppm and a tentative LOEL to be 750 ppm (highest dose tested), based on clinical signs of toxicity,

decreased food consumption and body weights, hematological effects, changes in clinical chemistries and histopathology in the liver, spleen and bone marrow. In the neurotoxicity phase of the same study, the NOEL for neurotoxic effects was 750 ppm. Decreased forelimb grip strength and decreased numbers of rears were considered to be secondary effects due to the decreased body weights and hematological effects.

In a subchronic feeding study in dogs, the NOEL was 100 ppm and the LOEL was 300 ppm, based on histopathological effects in the liver, spleen, and bone marrow.

In a subchronic dermal study in rats, the NOEL was 40 mg/kg/day and the LOEL was 200 mg/kg/day, based on hematological effects, increased liver weights, and histopathological effects in the liver. No dermal irritation was observed.

There were no developmental effects observed in the developmental toxicity study with rabbits. The maternal toxicity NOEL/LOEL were 10 and 20 mg/kg/day, respectively, based on tremors. In a developmental toxicity study with rats, developmental effects were observed at the highest dose tested, 180 mg/kg/day, including decreased fetal body weight and decreased ossification of caudal vertebrae and forelimb metacarpals. Maternal toxicity was observed also at the highest dose tested, 180 mg/kg/day, including increased mortality, decreases in food consumption and body weight, and hematological changes.

Several mutagenicity tests were all negative. These included an Ames assay with and without metabolic activation, an in vivo cytogenetic assay in rat bone marrow cells, an in vitro chromosome aberration assay in CHO cells, and a gene mutation assay with mammalian cells (HGPRT locus).

No Maximum Concentration Level for residues of Halofenozide in drinking water have been established. No food uses are proposed for Halofenozide. In fact this turf grass use is the only use anticipated for this pesticide. Additionaly EPA has commenced and nearly completed a process to identify a reasonable yet conservative bounding figure for the potential contribution of water related exposure to the aggregate risk posed by a pesticide. While EPA has not yet pinpointed the appropriate bounding figure for consumption of contaminated water, the ranges EPA is continuing to examine are all below the level that would cause Halofenozide to exceed the risk contributed to consumption of drinking water, if the registrations being considered in this memo are granted. EPA has therefore concluded that the potential exposure associated with Halofenozide in water, even at the higher levels EPA is considering as a conservative upper bound, would not prevent EPA from determining that there is a reasonable certainty of no harm if the proposed registrations are granted.

III. Ecological Effects

The environmental effects data are adequate to support the conditional registration of Halofenozide for use on turf grass. A summary of the ecological effects data is listed below:

The avian acute oral LD_{50} bobwhite quail was determined to be >2250 mg/kg. The avian dietary LC_{50}' for bobwhite quail was determined to be 3803 ppm and for mallard duck was determined to be >5000 ppm. Based on these values, Halofenozide is classified as practically non-toxic to bobwhite quail and mallard duck.

Halofenozide was found to affect reproduction in mallard ducks and bobwhite quail by significantly reducing egg production. The avian reproduction LOEC in bobwhite quail was 1000 ppm and the NOEC was 600 ppm. The avian reproduction LOEC in mallard ducks was 600 ppm and the NOEC was 300 ppm.

Acute toxicity for freshwater fish (Rainbow trout) (LC_{50}) was determined to be >8.6 ppm and for Bluegill sunfish was determined to be >8.4 ppm. Based on these data, Halofenozide is determined to be moderately toxic to freshwater fish on an acute basis.

Acute toxicity for Daphnia magna (EC_{50}) was determined to be 3.6 ppm. Based on these data, Halofenozide is classified as moderately toxic to Daphnia magna.

The mollusc shell deposition (Eastern Oyster) study showed an EC_{50} of 1.19 ppm. Based on these data, Halofenozide is moderately toxic to Eastern oyster.

Acute toxicity for estuarine invertebrates (Mysid Shrimp) (LC_{50}) was determined to be 3.5 ppm. Based on these data, Halofenozide is moderately toxic to Mysid Shrimp.

Acute toxicity for estuarine fish (Sheepshead Minnow) LC50 was determined to be >8.8 ppm. Based on these data Halofenozide is moderately toxic to Sheepshead Minnow.

The aquatic invertebrate life cycle (Daphnia magna) test indicated a NOEC of 30 ppb; a LOEC of 52 ppb; and a MATC of 39 ppb.

The estuarine/marine invertebrate life cycle (Mysidopsis bahia) study indicated a MATC between 50 ppb and 110 ppb. The geometric mean was 74 ppb.

The fish early life stage toxicity test in fathead minnows indicated a MATC between 0.45 and 0.97 ppm. The geometric mean MATC was 0.66 ppm.

The fish early life stage toxicity test in sheepshead minnow indicated a MATC between 1.6 and 3.1 ppm. The geometric mean MATC was 2.2 ppm.

Results of a freshwater green algae study indicate an EC_{50} of 0.78 ppm.

The honey bee LD_{50} was determined to be >100 ug/bee. Based on these data, Halofenozide is classified as practically non-toxic to honey bees.

Halofenozide is characterized as practically non-toxic to avian species on an acute oral and subacute basis, and mammals and honey bees on an acute basis. Halofenozide is moderately toxic to fish and invertebrates.

Summary of Ecological Risk to Non-endangered Organisms

The use of halofenozide on turf grass poses chronic risks to birds (impaired reproduction) and freshwater invertebrates. Chronic risks to freshwater fish cannot be assessed without additional data. An estuarine invertebrate chronic risk assessment has not been performed to date. A full ecological risk assessment cannot be completed because pertinent data are lacking.

Halofenozide is an insect growth regulator selectively targeted to arthropods that impacts growth and development (endocrine disruption). Reproductive impairment observed in birds and mammals with this compound and the related tebufenozide suggest possible vertebrate hormone modulation as well. Information presented by Canadian researchers at the 1996 annual Society of Environmental Toxicology and Chemistry (SETAC) meeting suggest that serious effects to aquatic species may occur from tebufenozide. Additional information (mesocosm field study) may be needed to fully evaluate this possibility for halofenozide (this information has already been submitted for tebufenozide). The mesocosm study is held in reserve pending receipt and review of the freshwater fish life-cycle study and relevant information on the related tebufenozide.

Summary of Ecological Risk to Endangered Organisms

Acute Levels Of Concern for endangered species are exceeded for birds. The Agency has concerns about the exposure of threatened and endangered species. Currently, the Agency is developing a program (The Endangered Species Protection Program) to identify all pesticides whose use may cause potential adverse impacts on endangered and threatened species and to implement mitigation measures that will eliminate the adverse impacts. The program will require users to consult county-specific bulletins. These bulletins will provide information about specific use restrictions to protect endangered and threatened species in the county of specific pesticide use. Consultations with the U.S. Fish and Wildlife Service will be necessary to assess risks to newly listed species or from proposed new uses.

The Agency plans to publish a description of the Endangered Species Protection Program in the Federal Register and have enforceable county-specific bulletins. Because the Agency is taking this approach for protection of endangered and threatened species, it is not imposing label modifications at this time. Rather, any requirement for product use modifications will occur in the future under the Endangered Species Protection Program.

IV. Environmental Fate

The environmental fate data are adequate to support the conditional registration of Halofenozide for use on turf grass. A summary of the environmental fate data is listed below:

Hydrolysis data indicate that Halofenozide is stable in the dark in sterile aqueous buffered solutions at pH 5,7, and 9.

Photodegradation in Water: Halofenozide did not significantly photodegrade in non-sterile pond water.

Photodegradation on soil: Halofenozide did not significantly photodegrade on soil under simulated sunlight conditions. The registrant calculated half-life was 129 days.

Aerobic soil metabolism: Halofenozide degraded with calculated half-lives of 68-72 days in a silt loam soil and 653-818 days in sandy loam soil.

Mobility (Batch Equilibrium): Halofenozide was mobile in sandy loam soil, silt loam soil, sand soil, and clay loam soil with adsorption Koc values ranging from 149-360 ml/g.

Anaerobic soil metabolism: Halofenozide did not degrade under anaerobic conditions preceded by 30 days of aerobic pre-incubation in a silt loam soil.

Bioaccumulation in fish: Halofenozide did not significantly bioaccumulate in bluegill sunfish when incubated for 28 days in a flow-through system containing 0.4 ppm halofenozide. Depuration was rapid and was essentially complete after 14 days of depuration.

Environmental Fate Assessment

Halofenozide has the potential to be mobile and very persistent in the environment. According to the data submitted by the registrant, halofenozide will not hydrolyze or photodegrade.

Halofenozide is soluble at approximately 12 ppm in water. Although the octanol water partition coefficient was determined to be 1654, indicating potential for bioaccumulation, the fish accumulation study showed low bioaccumulation and rapid depuration in bluegill sunfish.

Halofenozide has the potential to leach to ground water and to be transported in surface runoff. Halofenozide will be especially vulnerable to leaching since it will be applied to the top of established turf and moved into the root zone by watering in through rainfall or irrigation.

EFED recommended that the label include the following language: "This chemical demonstrates the properties and characteristics associated with chemicals detected in groundwater. The use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in groundwater contamination.".

Data gaps and Value of the Information.

a. **Environmental Fate.**

Aerobic soil metabolism (162-1). The study that was submitted was not acceptable because of the disparity in the aerobic soil metabolism half-lives. The registrant must provide an explanation for the ten-fold difference observed in the aerobic soil metabolism half-lives. In addition, to fulfill this data requirement, the registrant should submit aerobic soil metabolism rate studies done on at least ten different soils in an attempt to determine if the silt loam or sandy loam soil half-lives are typical of the degradation of halofenozide in the environment. These studies should be designed to track the degradation of the parent compound, and should not require radiolabeling or intensive sampling intervals.

Terrestrial field dissipation: soil (164-1). The studies that were submitted were not fully acceptable for this chemical because the registrant did not adequately consider the persistent nature of the chemical. The registrant stated that they are continuing to sample the bareground plots until 18 months post-application. This information must be submitted in order for these studies to fulfill Subdivision N guidelines.

Groundwater. The registrant must conduct prospective ground-water monitoring studies for halofenozide because of the persistent and mobile nature of the chemical. As the data base now stands, multiple ground water studies will probably be necessary to determine the potential groundwater contamination problems. In order to alleviate the need for additional expensive and potentially uninterpretable ground water studies, EFED recommends that the registrant submit additional field data on typical use sites as well as the aerobic soil metabolism rate studies (mentioned above). This information may be beneficial in determining the location of the groundwater studies and in interpreting the results.

b. **Ecological Effects.**

Freshwater Fish Life-Cycle (72-5). This study is needed to complete the data base and our understanding of the chronic risk to freshwater fish from halofenozide.

Aquatic field study (mesocosm). An aquatic field study (mesocosm) may be needed to evaluate potential invertebrate effects, but this requirement is held in reserve pending receipt and review of the freshwater fish life-cycle study and relevant information on related tebufenozide.

REGULATORY STATUS

- There are no pending regulatory actions against the registration of halofenozide for the proposed use pattern.

RECOMMENDATION

I recommend that you concur with the conditional registration under FIFRA Section 3(c)(7)(C) of the proposed manufacturing-use and end-use products containing the new chemical active ingredient, halofenozide, for the following reasons:

* Toxicology Branch II has determined that the existing database for halofenozide is adequate to support the Section 3 registration of the associated products for the proposed turf grass use pattern.

* It has been determined to be in the Public Interest to issue a conditional registion for halofeozide.

Concur: _____

Nonconcur: _____

Date: 5/20/97

Attachment: Pesticide Fact Sheet

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